

### **Remarks**

Claims 1, 2, 7-65, 80, 81, and 84-97 are pending in the application. Claims 21, 22, 26, 29, 31-36, and 38-45 have been withdrawn from consideration. Claims 1, 2, 7-20, 23-25, 27, 28, 30, 37, 46-65, 80, 81, and 84-97 are rejected.

Claims 2, 48-57, 81, and 92-95 have been canceled. New claim 98 has been added, and support for this new claim can be found in the specification at page 11, line 21–page 12, line 3. Claims 1, 62, 63, 85, 86, 90, and 94 have been amended, and support for these amendments can be found in original claims 50, 52, 56, and 57.

No new matter has been added by the present Amendment. Applicant respectfully requests reexamination and reconsideration of the case, as amended. Each of the rejections levied in the Office Action is addressed individually below.

**I. Rejection under 35 U.S.C. § 112, first paragraph.** Claims 92 and 95 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. Without conceding to the Examiner's position, Applicant has canceled claims 92 and 95 and, therefore, respectfully submits that the rejection is rendered moot by the present Amendment. Applicant reserves the right to pursue the canceled subject matter in future applications.

**II. Rejection under 35 U.S.C. § 103(a), as being unpatentable over Bernstein *et al.* (U.S. Patent 6,423,345).** Claims 1, 2, 7, 12-20, 23-25, 27, 28, 30, 37, 46-65, 80, 81, 84-97 are rejected under 35 U.S.C. 103(a) as being unpatentable over Bernstein *et al.* (U.S. Patent 6,423,345). The Examiner states that the particles of the present invention are obvious in view of Bernstein. Applicant disagrees.

The specification of Bernstein does not teach the microparticles of the present invention because the microparticles of Bernstein contain a synthetic polymer (column 3, line 36). In contrast, the specification of the present application *teaches away* from the use of synthetic polymers traditionally used in preparing microparticles for drug delivery. The present invention teaches the use of biocompatible components, such as lipids, proteins, and sugars, in the matrix of microparticles. Specifically, drug delivery particles containing PLGA were shown to elicit a

statistically significant increased inflammatory response at the site of injection compared to lipid-protein-sugar particles (page 52, sections entitled “Tissue reaction two weeks after injection” and “Tissue reaction eight weeks after injection”). In addition, PLGA particles were found at locations where they were not intentionally placed (page 54, section entitled “*Other findings on dissection*”). There were no similar adverse findings in rats injected with LPSPs. Given these negative consequences of administering a drug via microparticles comprising a synthetic polymer, *the present specification teaches away from particles which contain synthetic polymers*. This result is certainly surprising in light of the teaching of Bernstein, which states that “synthetic polymers are preferred due to more reproducible synthesis and degradation” (column 3, line 36).

Furthermore, the only microparticles that were actually produced by Bernstein contain only two components, PLGA and a lipid. The particles prepared by Bernstein do not contain a sugar or a protein, and the prepared particles always included a synthetic polymer (*i.e.* PLGA). Therefore, Bernstein does not teach or suggest microparticles which do not comprise a synthetic polymer such as PLGA. Applicant, therefore, submits that the present claims are not rendered obvious by the teachings of Bernstein and respectfully requests that the rejection be removed.

**III. Rejection under 35 U.S.C. § 103(a), as being unpatentable over Bernstein *et al.* (U.S. Patent 6,423,345) and further in view of Goldenheim *et al.* (U.S. Patent 6,534,081).** Claims 8-11 stand rejected by the Examiner under 35 U.S.C. § 103(a) as being unpatentable over Bernstein *et al.* (U.S. Patent 6,423,345), and further in view of Goldenheim *et al.* (U.S. Patent 6,534,081).

The Examiner only cites Goldenheim for teaching an anesthetic as the agent in the particles. As discussed above, Bernstein does not render obvious the claimed microparticles of the present application, and the combination of Goldenheim and Bernstein also does not teach the claimed microparticles. The claimed microparticles do not include synthetic polymers. Therefore, even if there is a teaching or suggestion to combine Goldenheim and Bernstein, the combination would not render the claimed invention of claims 8-11 obvious because the

references, even when combined, only teach a matrix comprising a synthetic polymer. Applicant, therefore, respectfully requests that the rejection be removed.

In view of the forgoing amendments and arguments, Applicant respectfully submits that the present case is now in condition for allowance. A Notice to that effect is requested.

If, at any time, it appears that a phone discussion would be helpful, the undersigned would greatly appreciate the opportunity to discuss such issues at the Examiner's convenience. The undersigned can be contacted at (617) 248-5215.

Please charge any fees that may be required for the processing of this Response, or credit any overpayments, to our Deposit Account No. 03-1721.

Respectfully submitted,



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